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TITLE: Breast Cancer Biomarkers in Nipple Aspirates From Women
Treated with Estrogen Receptor Blockers

PRINCIPAL INVESTIGATOR: Edward R. Sauter, M.D., Ph.D.

CONTRACTING ORGANIZATION: Thomas Jefferson University
Philadelphia, Pennsylvania 19107

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INTRODUCTION

We are enrolling postmenopausal women at increased breast cancer risk who have entered the Study of Tamoxifen and Raloxifene (STAR) trial. Our study collects nipple aspirate fluid (NAF) prior to starting and 6 months after initiating tamoxifen (TAM) or raloxifene (RAL), as called for by the STAR trial. The purpose of our study is to determine if 1) success in collecting NAF increases with experience, 2) NAF biomarkers (cytology, ploidy, cell cycle parameters, and prostate-specific antigen, PSA) change in response to treatment with TAM or RAL, and 3) NAF biomarker changes are associated with future breast cancer risk. Our hypothesis is that NAF biomarkers will respond to treatment with TAM or RAL, and that biomarker change(s) will predate clinical findings observed on mammography or physical examination. This multiinstitutional trial currently involves three centers (Thomas Jefferson University, UCLA and Fox Chase Cancer Center). If our hypothesis proves correct, then nipple aspiration may provide a useful noninvasive method to evaluate response to treatment.

BODY

Below we address each task in the approved Statement of Work.

Task 1. Evaluate the success of dedicated individuals in performing nipple aspiration (Months 1-32).

A. Notify physicians at Thomas Jefferson University and its Network Hospitals, as well as at the University of California at Los Angeles (UCLA) and its participating institutions, that the study has begun (Months 1-3).

This has been done. We now have a third institution, Fox Chase Cancer Center, that is part of the study.

B. Dr. Sauter to UCLA to insure consistency among institutions in the nipple aspirate technique.

UCLA hired a nurse experienced in nipple aspiration whom I observed in 1999. Both the nurse coordinator at Jefferson and I have trained the nurse coordinator at Fox Chase to perform nipple aspiration. The success in collecting NAF at each institution is as follows:

Institution	Subjects	Visits
TJU	12/13	18/19
UCLA	3/3	6/6
Fox Chase	4/4	5/5
Totals	19/20(95%)	29/30(97%)

C. Enroll subjects for initial (Months 1-28) and repeat aspirations (Months 7-34).

This is ongoing.

D. Work with the data management programmers to establish data entry files for use by participating research laboratories (Months 1-6).

This has been done.

E. Evaluate the success of collecting nipple aspirate fluid during years 1, 2, and 3 (Months 24-36).

Please see response to B above. NAF not obtained from only one individual consented to enroll in year 1 of the study.

Task 2. Assess biomarkers obtained in samples

A. Begin evaluation of NAF specimens. Evaluate NAF cytology, ploidy, cell cycle parameters, and PSA (Months 1-32).

We have done this. Our sample size is insufficient for statistical analysis.

B. Finalize the analysis of specimens. Compare results at baseline vs. treated samples.

This will be performed later.

C. Prepare an outline of NAF biomarkers which indicates how frequently and in which direction (favorable or unfavorable) each has changed after treatment.

This will be done when the sample size is larger.

D. For each biomarker, determine if there is an association between a biomarker change after treatment with tamoxifen/raloxifene and risk of precancer/cancer in the breast. This determination will be made in Month 36 of the study and after all subjects have received 5 years of treatment.

This will be done later.

KEY RESEARCH ACCOMPLISHMENTS

- Preliminary evidence that nipple aspiration can be successfully taught and performed by health care providers at multiple institutions
- Recruitment of subjects at increased breast cancer risk enrolled on the STAR trial at multiple institutions with limited funding
- NAF sample analysis performed by experts at multiple institutions

REPORTABLE OUTCOMES

1. IRB approval at Thomas Jefferson University, UCLA, Fox Chase Cancer Center and Ellis Fischel Cancer Center
2. 20 subjects enrolled, and 12 have completed the trial.
3. evaluation of all biomarkers for ????
4. successful NAF collection from 95% of subjects and 97% of visits

CONCLUSIONS

Our preliminary findings demonstrate that nipple aspiration can be learned and successfully performed at multiple institutions, indicating that it is feasible to perform the procedure on a wide scale, should useful biomarkers be identified.

REFERENCES

Ehya H, Iacono R, Klein-Szanto AJP, James J, Daly MB, Sauter ER. Breast Cancer Biomarkers In Nipple Aspirates From Women Treated With Estrogen Receptor Blockers. Department of Defense Breast Cancer Research Program Mtg, 2002.

APPENDICES N/A